ACTIVE GLAUCOMA OR AN OLD INSULT?

Clinicians discuss the diagnosis and therapeutic considerations.

BY DEVESH K. VARMA, FRCSC; REENA A. GARG, MD; AND MICHAEL D. GREENWOOD, MD

CASE PRESENTATION

A 47-year-old woman with myopia was referred for a glaucoma evaluation. The patient had undergone LASIK surgery 20 years earlier. She visited her optometrist regularly, and IOP readings were always approximately 12 mm Hg OU. Changes to the optic nerve had been attributed to myopia and physiologic cupping. In 2018, she experienced an aortic dissection that resulted in marked systemic hypotension and a watershed infarct affecting her right frontoparietal lobe. Since that episode, she had been on a regimen of candesartan and bisoprolol.

On examination, IOP was 12 mm Hg OU. Central corneal thickness was 605 µm OD and 444 µm OS. Corneal hysteresis was 8.5 OD and 11.1 OS, suggesting a corrected Goldmann IOP of 11.6 mm Hg OD and 12.4 mm Hg OS. The angle in each eye was open to the ciliary body on gonioscopy, and this was confirmed with anterior segment imaging (Figure 1). In both eyes, disc cupping was marked (Figure 2), and significant damage to the retinal nerve fiber layer was evident superiorly and inferiorly (Figure 3). Disc photographs taken by the referring optometrist before the aortic dissection in 2018 showed a similar degree of cupping. Visual field (VF) testing showed fixation-splitting superior loss in both eyes, although reliability was poor for the right eye because of numerous fixation losses (Figure 4). No previous VF tests or OCT images were available for comparison.

Further testing was performed to explore potential non–IOP-dependent mechanisms for optic neuropathy. An MRI showed evidence of the previous right frontoparietal infarct and ruled out compressive optic neuropathy. Bloodwork, including a complete blood count, a vitamin B12 test, an antinuclear antibody test, an erythrocyte sedimentation rate, and a thyroid-stimulating hormone test, was normal. The patient declined a sleep study, but the index of suspicion for sleep apnea was low given her lack of sleepiness and snoring and her lean body

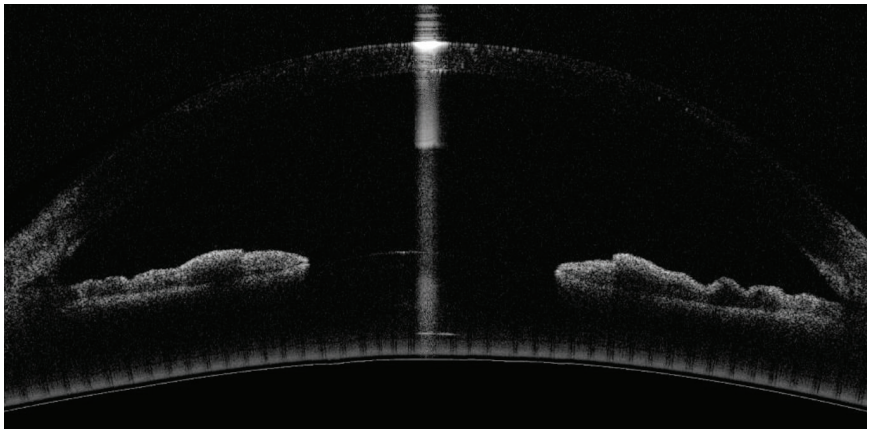

Figure 1. Anterior segment OCT imaging of the right eye confirmed that the angle was open. Results for the left eye were similar.

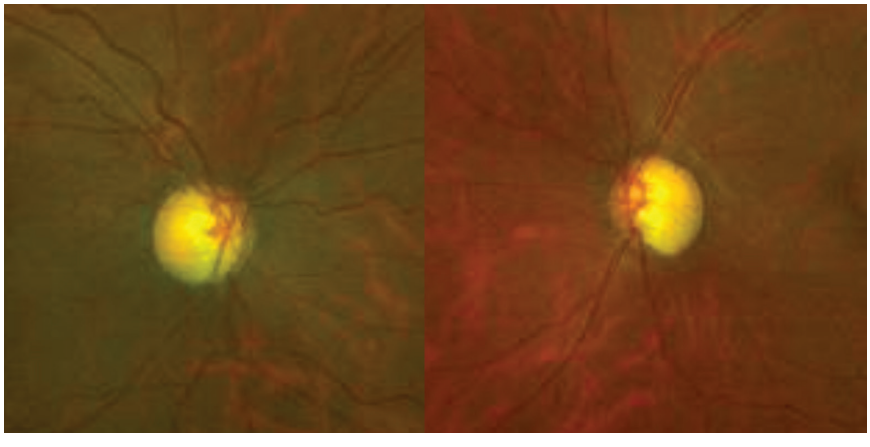

Figure 2. Optic nerve photography showed marked cupping in each eye.

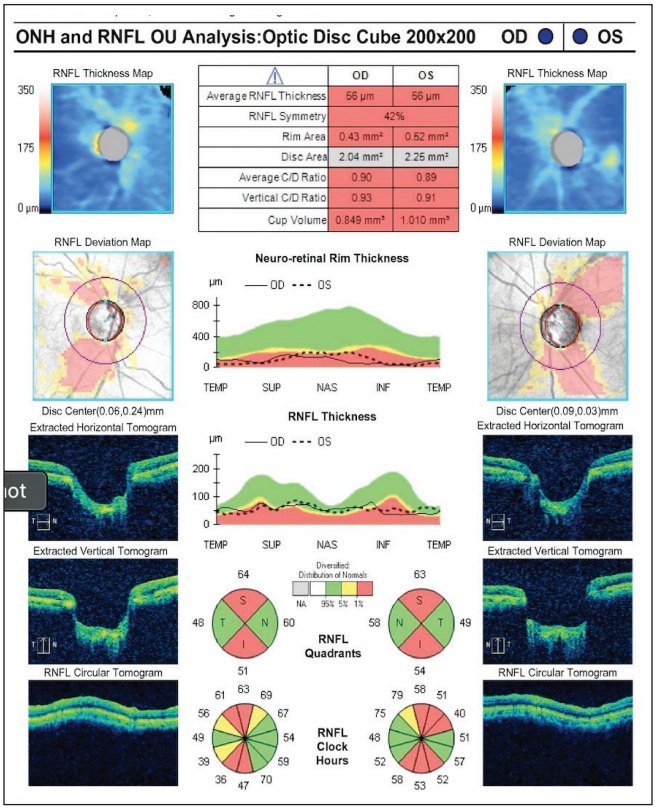

Figure 3. OCT imaging of the optic nerves showed significant retinal nerve fiber layer loss superiorly and inferiorly in each eye.

habitus. A 24-hour blood pressure study showed nocturnal diastolic dipping to 40 mm Hg.

The patient asked, "What happened to me?" and "What do we need to do?" These are both excellent questions. Is this normal-tension glaucoma (NTG), optic neuropathy from a hypotensive episode in 2018, a combination of both, or something else entirely? Should IOP-lowering therapy be initiated, or may she be safely observed, with treatment initiated only if further damage occurs? If you recommend starting treatment, what is an appropriate target IOP, and what first-line treatment would you offer? If you recommend observation, which tests are the most appropriate for detecting disease progression, and are any additional tests or avenues worth exploring to establish her diagnosis?

–Case prepared by Devesh K. Varma, FRCSC

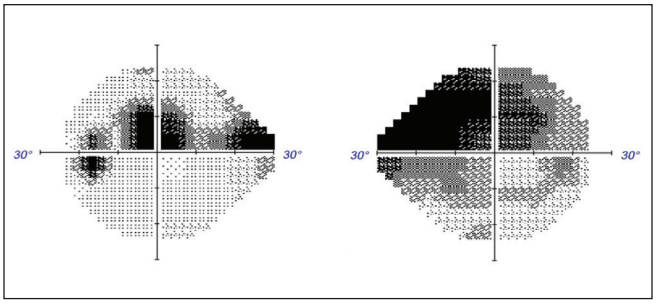

Figure 4. Humphrey VF testing (Carl Zeiss Meditec) showed advanced fixation-splitting superior field loss that was worse in the right eye.

REENA A. GARG, MD

This case presents a diagnostic and treatment dilemma in a young patient with a complicated history. Her discs, OCT scans, and VF tests are all suspicious for NTG, but the discs appear to be reassuringly stable since before the vascular incident. It would be helpful to evaluate earlier VF tests for changes before 2018 and to determine whether, if changes occurred, they were progressive.

I am not reassured by this patient's low IOP readings, even after correction for hysteresis. She is clearly susceptible to optic nerve damage, whether because of the incident in 2018 or from NTG. I rarely obtain diurnal IOP measurements, but they would be helpful in this case. If she is experiencing wide swings in IOP, I might initiate therapy with a Rho kinase inhibitor to stabilize the IOP. A reduction in episcleral venous pressure with this medication would be an added benefit. I would also ask the patient to consider administering her blood pressure medications in the morning to mitigate some of the nocturnal hypotension she is experiencing.

Most important, I would have a frank conversation with the patient about her situation. She is young, and the prognosis of patients with advanced NTG isn't great. Given the natural course of this disease, I would monitor her closely but proceed conservatively, especially given her comorbidities.

MICHAEL D. GREENWOOD, MD

With few historical glaucoma tests available, the similarity in the optic nerves' appearances before and after the aortic dissection is helpful. IOP measurements after LASIK can be unreliable. Using the Ocular Response Analyzer (Reichert) helps to confirm the IOP readings, and corneal hysteresis measurements indicate that the right eye is at greater risk of disease progression than the left eye.

The true cause of this patient's VF loss may never be known, but I suspect NTG. I would not initiate IOP-lowering

therapy at this time. Instead, I would observe her closely with multiple VF tests and OCT scans to determine if there is active progression. I would be comfortable with close monitoring to start because, in the Collaborative Normal Tension Glaucoma (CNTG) study, more than half of the participants did not experience disease progression.[1]

If I were to initiate medical therapy, I would consider netarsudil ophthalmic solution 0.02% (Rhopressa, Aerie Pharmaceuticals) or latanoprostene bunod ophthalmic solution 0.024% (Vyzulta, Bausch + Lomb) because they might lower episcleral venous pressure and reduce IOP in a patient whose starting IOP is already low. I would encourage the patient to administer her systemic antihypertension medications in the morning to reduce nighttime hypotension.

Further testing would include diurnal IOP measurement to ensure that she is not experiencing IOP spikes. I would also want to review previous measurements of cerebrospinal fluid pressure if available. Patients with NTG tend to have lower cerebrospinal fluid pressure than normal patients and patients with ocular hypertension,[2,3] so these measurements could shed light on this case and help guide future therapy.

WHAT I DID: DEVESH K. VARMA, MD, FRCSC

Because disc photographs taken before and after the hypotensive episode in 2018 showed similar degrees of optic nerve cupping, my diagnosis was underlying advanced NTG. Although the patient had experienced a right frontoparietal stroke from hypotension, the left inferior VF quadrants remained intact, so I suspected that the stroke had had little impact on her optic radiations. The hypotensive episode that injured the frontoparietal lobe, however, might also have caused an injury elsewhere, including the optic nerves, so an acute or chronic injury was a reasonable working hypothesis. The nocturnal diastolic dipping was likely indicative of long-standing mechanisms unrelated to IOP that were contributing to glaucoma.

I began by adjusting the patient's antihypertensive medications in consultation with her family doctor. The patient was already administering both medications in the morning, so no change in schedule was required. Her family doctor agreed to halve the candesartan dose. Although the IOP had always measured approximately 12 mm Hg, I thought that a more complete picture of the patient's 24-hour IOP might be helpful. She used an Icare Home Tonometer (Icare USA) for 1 week to better elucidate her IOP pattern (Figure 5). The testing confirmed significant IOP fluctuations, with higher pressures in the right eye

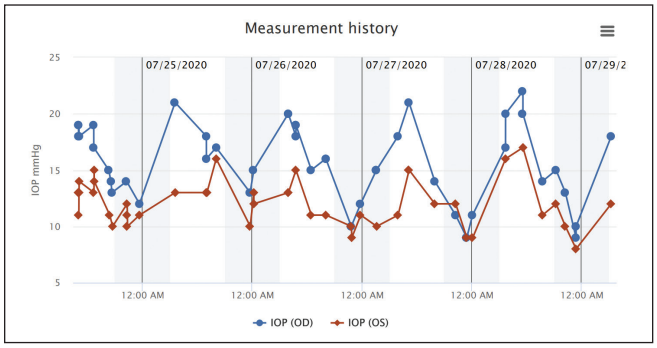

Figure 5. Measurements with the Icare Home Tonometer reveal significant IOP fluctuations and high peaks in IOP in the right eye.

and a peak of 22 mm Hg. The lowest pressures were measured at night when her diastolic blood pressure was also at its lowest.

The patient is scheduled to return to discuss the results of home tonometry. At that time, I will recommend initiating IOP-lowering therapy with an aim of reducing mean IOP by 30% and blunting IOP fluctuations. Her options for first-line treatment include laser trabeculoplasty and topical therapy. In addition to the side effects, we will discuss the theoretical benefits of different options for topical therapy such as a possible improvement in blood flow with a carbonic anhydrase inhibitor or nitric oxide–releasing drop and a theoretical potential for neuroprotection with an alpha agonist. Fortunately, despite her advanced disease, this patient has multiple options. ■

1. Anderson DR; Normal Tension Glaucoma Study. Collaborative Normal Tension Glaucoma Study. *Curr Opin Ophthalmol*. 2003;14(2):86-90.
2. Ren R, Jonas JB, Tian G, et al. Cerebrospinal fluid pressure in glaucoma: a prospective study. *Ophthalmology*. 2010;117(2):259-266.
3. Berdahl JP, Allingham RR, Johnson DH. Cerebrospinal fluid pressure is decreased in primary open-angle glaucoma. *Ophthalmology*. 2008;115(5):763-768.

DEVESH K. VARMA, MD, FRCSC | SECTION EDITOR
- Glaucoma and advanced anterior segment surgeon, Prism Eye Institute, Mississauga, Ontario, Canada
- Assistant Professor, University of Toronto
- Member, *Glaucoma Today* Editorial Advisory Board
- devesh.varma@prismeye.ca
- Financial disclosure: None

REENA A. GARG, MD
- Glaucoma specialist, Washington Eye Institute, Greenbelt, Maryland
- Residency Program Director, Medstar Washington Hospital Center/Georgetown University, Washington, DC
- ragarg927@gmail.com
- Financial disclosure: Speaker fees (Aerie Pharmaceuticals, Bausch + Lomb)

MICHAEL D. GREENWOOD, MD
- Glaucoma, cornea, cataract, and refractive surgery specialist, Vance Thompson Vision, Fargo, North Dakota
- michael.greenwood@vancethompsonvision.com; Twitter @migreenw
- Financial disclosure: Research support and speaker fees (Aerie Pharmaceuticals)